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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,721	07/11/2001	Bruce Acres	017753-132	7786

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BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,721	ACRES ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,20,21 and 23-30* is/are pending in the application.

4a) Of the above claim(s) *11-17,20,23-25 and 27-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,21,26 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4/4/01* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/18/2004 has been entered.

Claims 1 and 7 have been amended. Claims 18, 19, and 22 have been canceled. Claims 11-17, 20, 23-25, and 27-29 are withdrawn from consideration. Claims 1-10, 21, 26, and 30 are under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims or arguments or new grounds of rejections will not be reiterated. The arguments in 12/12/03 response would be addressed to the extent that they apply to current rejection.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific

reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Specification

The abstract of the disclosure is objected to because words such as "concerns" and "said" are used. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Objections

Claim 1 is objected to because it appears that "all of part" in line 8 should be replaced with "all or part".

Claim 10 is objected to because of the following informalities: gp16O should be replaced by "gp160". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 21, 26, and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite because claim 1 recites, "a promoter and/or regulatory sequence". The claim as written encompasses a nucleic acid that does not contain a promoter but only a regulatory sequence. It is unclear whether applicants intend to claim such a nucleic acid, thus, the metes and bonds of the claims are uncertain.

Claim 3 recites the limitation "said target cells". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 7-9, 21, and 30 are newly rejected under 35 U.S.C. 102(b) as being anticipated by *Hayden et al* (Tissue Antigens 1996;48:242-54), and as evidenced by *Janeway, Jr.* (Immunobiol 1999).

Hayden et al teach a biological material i.e. either an expression cassette (a naked DNA sequence) or a retroviral vector comprising the expression cassette containing a promoter (CMV promoter) operably linked to a gene of therapeutic interest that encodes heavy and light chain of a single chain antibody (e.g. fig. 1) that recognizes CD28 (capable of binding to a polypeptide that is part of the TCR complex), and fused to a cell receptor (CD80) transmembrane polypeptide (2e12-Ig-B7-1 fusion cassette and hulgG1-CD80 fusion cassette, right column, 2nd Section, page 243). *Hayden et al* also teach transducing human tumor cells (the target mammalian cell) with the expression vectors for cancer immune therapy (e.g. abstract). Although not relied upon, *Janeway, Jr.* teaches that the CD28 receptor consists of TCR-α and TCR-β chains (§ 4-23, and Fig. 8.10). Accordingly, *Hayden et al* anticipate instant claims.

Claims 1-9, 21, 26, and 30 are newly rejected under 35 U.S.C. 102(e) as being anticipated by *Ledbetter et al* (US 6,699,715), and as evidenced by *Gilliland et al* (Tissue Antigens 1996;47:1-20).

Ledbetter et al teach a biological material comprising a modified single chain variant (sFv) molecule containing a binding site of an antibody and at least a portion of a transmembrane domain of a cell receptor, preferably the antibody recognizes a TCR complex CD28 receptor, and contains both heavy and light chains V_H and V_L (column 1,

lines 47-64), wherein other TCR complex such as CD3 is also encompassed by the cited patent (column 5, lines 15-17). Although not relied upon, *Gilliland et al* teach rapid and reliable cloning of sFv antibodies against various TCR complexes, which establishes that the state of the art is well developed at the time in making the various anti-TCR antibodies contemplated in the cited patent. *Ledbetter et al* go on to teach nucleic acids and vectors encoding the modified sFv molecule (e.g. figures 10-13 and columns 8-12), wherein the vector could be naked DNA or RNA sequences or recombinant viral vectors. *Ledbetter et al* go on to teach introducing the nucleic acid molecules encoding the modified sFv molecule into mammalian target cells, wherein the nucleic acids could be complexed with cationic lipids to facilitate the transfection process (column 10, lines 44-48). *Ledbetter et al* teach that the molecule is useful for enhancing an immune response against a disease (column 1, lines 36-50). Accordingly, *Ledbetter et al* anticipate the instant claims.

Claims 1-3, and 30 stand rejected under 35 U.S.C. 102(e) as being anticipated by *Wittrup et al* (US 6,423,538), and as evidenced by *Lu et al* (Biochim Biophys Acta 2000;1491:13-9), for reasons of record and following.

Applicants argue that *Wittrup et al* expressing the antibody in yeast cells, and a yeast cell is not considered as the target cell.

In response, the claims are drawn to a biological material comprising at least one nucleic acid sequence. The newly added limitation, "wherein said target cell is a mammalian cell" states the intended use of the nucleic acid sequence, but do not place

any limitation on the structure of the nucleic acid sequence itself. Since the promoter GAL-1 disclosed by *Wittrup et al* is also functional in mammalian cells as evidenced by *Lu et al*, the rejection stands.

Please note that intended use limitations bear little weight on the determination of novelty of the invention. This is because a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. **If the prior art structure is capable of performing the intended use, then it meets the claim.** In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Claims 1-3 stand rejected and claim 21 is newly rejected under 35 U.S.C. 102(a) & (e) as being anticipated by *Burkly et al* (US 5,871,732), and evidenced by *Janeway, Jr. et al* (Immunobiology, 1999), for reasons of record and following.

Claim 21 is drawn to combining a pharmaceutically acceptable carrier with the biological material of claim 1. *Burkly et al* teach such in column 20, line 45.

Applicants argue that it is not apparent that the Janeway publication disclosed that CD4 comprises TCR-alpha and TCR-beta, and submitted Cruse et al reference teaching that CD4 is a single chain glycoprotein.

In response, the claims now standing rejected are not limited to TCR-complex that comprises TCR-alpha and TCR-beta. Thus, the rejection stands.

Claims 1-6, 21, 26, and 30 stand rejected under 35 U.S.C. 102(e) as being anticipated by *German et al* (US 6,531,455), for reasons of record and following.

Applicants argue that German et al disclose methods for delivering a polypeptide to the bloodstream, the nucleic acid construct of German et al does not comprise a region which allows the anchoring to the cell membrane, whereas the presently claimed invention allows the expression of an antibody at the surface of the target cell.

In response, the argument is moot because the instantly rejected claims do not contain the limitation of comprising a membrane-anchoring sequence. Thus, *German et al* meets claim limitation, and the rejection stands.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 7, 9, 10 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Ledbetter et al* (US 6,699,715), in view of *Allison et al* (US 5,811,097), *Gupta et al* (DNA Cell Biol 1998 Jul;17:573-81), and *Antoine et al* (Virol 1998 May;244:365-96).

Claim 5 recites an option of using MVA as the viral vector of choice. Claim 10 is drawn to fusing the transmembrane polypeptide of CD4 or rabies virus glycorprotein with the antibody heavy chain.

Ledbetter et al teaches the importance of using a transmembrane domain to anchor the sFv molecule to the cell membrane (column 1, lines 36-54), the illustrated transmembrane domain of *Ledbetter et al* is from CD80 (e.g. fig. 7). *Ledbetter et al* teaches numerous recombinant viral vectors known in the art, but does not specify the MVA vector, nor set forth a list of transmembrane molecules known in the art.

Allison et al and *Gupta et al* supplemented *Ledbetter et al* by teaching other transmembrane polypeptides known in the art. *Allison et al* teach using a transmembrane domain to anchor a peptide on the cell membrane when peptide expression on the surface of the cell is desired, wherein the transmembrane domain could be obtained from cell surface proteins other than the peptide such as the transmembrane peptides of CD4 and CD8 (column 6, lines 48-55). *Gupta et al* teach that the glycoprotein of rabies virus is a good candidate for membrane anchoring sequence in a fusion protein intended to be expressed on the cell surface (e.g. abstract). *Antoine* reference establishes that the modified virus Ankara (MVA) is well known in the art as the vaccine carrier, and that the rabies glycoprotein could be constructed in such a recombinant construct.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the nucleic acid taught by *Ledbetter et al* by simply substituting the transmembrane polypeptide of CD80 with that of CD4 or rabies

glycoprotein as taught by *Allison et al* and *Gupta et al* in an art known recombinant MVA viral vector construct as taught by *Antoine et al* with a reasonable expectation of success. Given the knowledge of the reasonable skilled, these limitations would fall within the bounds of the optimization, i.e. selecting a suitable transmembrane region known in the art to anchor the single chain antibody on cell membrane, and selecting a suitable viral vector as the carrier for transgene delivery. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

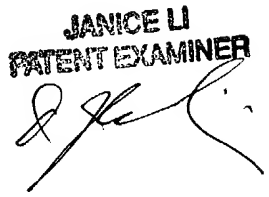
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist **Rena Jones** whose telephone number is **571-272-0571**.



Q. Janice Li
Patent Examiner
Art Unit 1632

QJL
April 26, 2004